Brief Comm

Title: Ethylene glycol (EG) - estrogen receptor binding assay //////

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Abstract

Ethylene glycol was tested in a standard competitive ligand binding assay for the estrogen receptor. At concentrations of 0.3, 1.0, 3.0, and 10.0% (v/v) EG in phosphate buffered saline, no competitive or non-competitive inhibition was observed. It is concluded that EG does not bind to the estrogen receptor.

There has been increasing focus on the potential for chemicals to affect the endocrine system. Of particular interest, are chemicals that can bind to endogenous endocrine receptors thus potentially resulting in effects at lower concentrations than might otherwise be observed. Primary among the receptors of interest is the estrogen receptor and a wide variety of assays have been employed to evaluate so called "estrogenicity" of chemicals [1]. In a previous "Brief Communication" in this journal, Ren et al. [2] reported that two solvents, dimethyl formamide (DMF) and EG, when injected into fish at high concentrations (>4 gm/kg), induced the mRNA of the egg protein vitellogenin. Vitellogenin induction has been used elsewhere as a monitor for estrogen-like activity [3].

A standard competitive ligand binding assay for ^{3}H-estradiol with its receptor was conducted for EG. EG at four concentrations, 0.3, 1.0, 3.0, and 10.0% (v/v) in phosphate buffered saline, was tested for its ability to competitively replace ^{3}H-estradiol from the calf uterus estrogen receptor. Inhibition at the four concentrations was recorded as 2, 3, 5 and 5%, respectively. It was concluded that EG does not bind to the estrogen receptor, (approximately 50% inhibition and dose response is considered necessary for a positive response).

We have discussed in other places [4] the ramifications of the binding of chemicals with structures as dissimilar as EG and DMF are from the natural ligands of the estrogen receptor. It was deemed important to determine if EG could, indeed, be inducing mRNA of vitellogenin through the defined mechanism of acting as a ligand for the receptor. As predicted from its structure, no such binding occurred even at concentrations which might have resulted in non-competitive displacement [1]. It is therefore, presumed that the response previously reported in fish [2] from very high concentrations of EG result from other phenomena and EG is not "estrogenic".

More recently, one of the authors of the original Brief Communication, has written to this journal suggesting that the original results are not due to "estrogenicity" of EG. [5] It is interesting to speculate on potential causes for mRNA induction in these fish (e.g. stress, contamination, or normal processes), whether vitellogenin itself was actually

induced, and, indeed, the broader question of why male fish have retained the capability of vitellogenin production through evolution. The mRNA of vitellogenin can, apparently, be induced by a number of environmental factors including temperature changes (J. Lech